March 15, 2001

Edwin L. Mongan III
Manager, Environmental Stewardship
DuPont SHE Excellence Center
1007 Market Street
Wilmington, DE 19898

Dear Mr. Mongan:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Dimethyl ether (CAS No. 115-10-6), posted by EPA on November 20, 2000. I commend the DuPont Corporation for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Chemical RTK HPV Challenge Program website EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

As detailed in the attached Comments, DuPont needs to supply additional information on the ecotoxicity studies. The fish and invertebrate robust summaries contain insufficient information to permit an assessment of data adequacy. The submitted algal predicted value using ECOSAR is acceptable for determining the hazard associated with algae, provided that a robust summary of experimental data for an appropriate analog chemical is submitted to support the ECOSAR value in a manner consistent with the EPA Challenge guidance for applying structure-activity relationships (http://www.epa.gov/opptintr/chemrtk/sarfinl1.htm).

In addition, DuPont needs to supply the assumptions and data inputs for transport/distribution modeling. Some information needs to be added to two robust summaries for health effects, and editorial errors including placement of information in the fate summary format need to be corrected.

As with other submissions where the available data are either inadequate or insufficiently documented, this case will remain open until adequate documentation is in hand.

EPA will post this letter and the attached Comments on the Chemical RTK web site within the next few days. As noted in the comments, we ask that DuPont advise the Agency, within 60 days of the posting on the Chemical RTK website, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-260-3470. Submit general questions about the HPV Challenge Program through the Chemical RTK web site comment button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@.epa.gov.

I thank you for your submissions and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Attachment

cc: W. Sanders
C. Auer
M. E. Weber
A. Abramson

EPA Comments on Chemical RTK HPV Challenge Submission: Dimethyl Ether

SUMMARY OF EPA COMMENTS

The sponsor, DuPont Corporation, submitted a Test Plan and Robust Summaries to EPA, received October 31, 2000, for Dimethyl ether (CAS # 115-10-6). EPA posted the submission on the RTK HPV Challenge Web site on November 20, 2000.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical and Environmental Fate Data. All appropriate SIDS-level tests have been performed. The sponsor needs to address a few deficiencies in the robust summaries; see "Specific Comments on Robust Summaries."

2. Health Endpoints: All appropriate SIDS-level tests have been performed. The sponsor needs to address deficiencies in the developmental toxicity robust summary; see "Specific Comments on Robust Summaries."

3. Ecotoxicity. The robust summaries for fish and invertebrate studies are inadequate for the purpose of the U.S. HPV Challenge Program. Without the missing information, EPA cannot evaluate the proposal with respect to this endpoint. The submitted algal predicted value using ECOSAR will be acceptable for determining the hazard associated with algae, provided that the sponsor submits a robust summary of experimental data for an appropriate analog chemical to support the value.

EPA is requesting that the Sponsor advise the Agency within 60 days of any modifications to its submission.

EPA COMMENTS ON THE DIMETHYL ETHER CHALLENGE SUBMISSION

Test Plan

Chemistry (melting point, boiling point, vapor pressure, water solubility, and partition coefficient).

Adequate existing data are available for these endpoints.

Fate (photodegradation, stability in water, biodegradation, and transport/distribution).

Adequate existing data are available for these endpoints.

Health Effects (acute toxicity, repeat dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

Adequate existing data are available for these endpoints.

Ecological Effects.

Deficiencies in the summaries for the existing fish and invertebrate studies need to be remedied before EPA can determine the adequacy of the data (see following section).

The submitted algal predicted value using ECOSAR is acceptable for determining the hazard associated with algae, provided that a robust summary of experimental data for an appropriate analog chemical is submitted to support the ECOSAR value in a manner consistent with the EPA Challenge guidance for applying structure-activity relationships (http://www.epa.gov/opptintr/chemrtk/sarfinl1.htm).

SPECIFIC COMMENTS ON ROBUST SUMMARIES

Chemistry

Physicochemical data agree with independent sources. However, the water solubility value was determined at a pressure of 5 atmospheres and is therefore not the most appropriately measured value for determining the environmental fate of a compound. Additionally, the magnitude of the value reported by the sponsor should have been reported as 10^5 rather than 10^4. A preferred value for water solubility, determined at standard temperature and pressure, is 4.6×10^4 ppm (J. Hine & P. K. Mookerjee, J. Org. Chem. 40: 292-298 (1975)).

Fate

Some entries were misplaced. The hydrolysis of dimethyl ether was addressed in the "Photodegradation" section of the document rather than under "Stability in Water", and volatilization from moist and dry soil surfaces was addressed under the "Stability in Water" section of the document rather than in the "Transport" section. The sponsor needs to correct these deficiencies in order to provide acceptable documentation for the Challenge program.

The water solubility value referenced in the document was not the most appropriately measured value for determining the environmental fate of a compound (see under Chemistry, above). However, while using the suggested alternative value to calculate the Henry's Law Constant provides a different numerical result, the amended values do not change the interpretation of the data.

The sponsor's treatment of fugacity is adequate, except that the sponsor needs to provide the assumption and data inputs to the model (see Guidance for Robust Summary preparation).

Health Effects

EPA received nine health endpoint robust summaries and found one of them (developmental toxicity summary) to be deficient for the purposes of the U.S. HPV Challenge Program.

The following EPA comments reflect the information in the robust summary (the full study report may address these comments):

Repeat Dose/Reproductive Toxicity: EPA notes that the sponsor has used a two-year cancer bioassay to meet the SIDS-level testing requirements for repeat dose toxicity and reproductive toxicity. It is clear that this study meets both SIDS endpoints and that the protocol used was appropriate. However, the conclusion by the sponsor that the mammary masses/tumors observed were not treatment-related due to the incidence for these tumors in the controls being uncharacteristically low needs to be substantiated further. EPA requests that the incidence data by dose, statistical information and historical control data for these effects be provided so an independent analysis of the data can be made.

Developmental Toxicity Study: This robust summary is considered deficient because it did not provide the incidence by dose (and statistical analyses) for the skeletal variations observed. EPA also found this summary confusing. For example, the total number of live fetuses is presented differently in the first and second tables of the summary and several parameters (including the number of fetuses and sex ratios) are not provided. Thus, the sponsor needs to provide all of the aforementioned information to allow for an independent analysis of the data . Finally, EPA suggests that clarification be provided as to why there are two experiments (designated Part I and Part II) and whether they were done concurrently or sequentially.

Ecotoxicity Studies

The comments below reflect the information presented in the robust summaries; information in the full study report may address some of the issues identified.

Acute Aquatic Toxicity. Three robust summaries were submitted for studies on fish, daphnia, and green algae.

Robust summaries-fish and daphnid. The two robust summaries submitted for fish and daphnid acute data were inadequate. Information lacking for these two endpoints includes: pH, DO, TOC, temperature, number of replicates per test, purity, percent concentration recovered at the end of the tests, and water hardness. Without this information, reviewers cannot determine the adequacy of the data. Thus, the sponsor needs to provide the missing robust summary information for these acute studies.

Robust summary–aquatic plant. The submitted algal predicted value using ECOSAR is acceptable for determining the hazard associated with algae, provided that a robust summary of experimental data for an appropriate analog chemical is submitted to support the value.

Followup Activity

EPA requests that the Sponsor advise the Agency within 60 days of any modifications to its submission.